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L5: Entry 1 of 1 File: DWPI Sep 17, 2002

DERWENT-ACC-NO: 2000-053228
DERWENT-WEEK: 200276

TITLE: Ultradisperse nanoparticles of hydrated oxide for use in structuring three-sided biological system

INVENTOR: CHUIKO, A; DICKSTEIN, S ; INGMAN, D ; OGENKO, V

PATENT-ASSIGNEE:

ASSIGNEE	CODE
BIO-SEAL LTD	BIOSN

PRIORITY-DATA: 1998US-086261P (May 21, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2002530270 W	September 17, 2002		070	A61K009/14
WO 9959811 A1	November 25, 1999	E	066	B32B005/16
AU 9939531 A	December 6, 1999		000	B32B005/16
EP 1089872 A1	April 11, 2001	E	000	B32B005/16
BR 9910623 A	October 23, 2001		000	B32B005/16
CN 1307522 A	August 8, 2001		000	B32B005/16
KR 2001081960 A	August 29, 2001		000	A61K009/51

DESIGNATED-STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
JP2002530270W	May 20, 1999	1999WO-IL00272	
JP2002530270W	May 20, 1999	2000JP-0549458	
JP2002530270W		WO 9959811	Based on
WO 9959811A1	May 20, 1999	1999WO-IL00272	
AU 9939531A	May 20, 1999	1999AU-0039531	
AU 9939531A		WO 9959811	Based on
EP 1089872A1	May 20, 1999	1999EP-0922473	
EP 1089872A1	May 20, 1999	1999WO-IL00272	
EP 1089872A1		WO 9959811	Based on
BR 9910623A	May 20, 1999	1999BR-0010623	
BR 9910623A	May 20, 1999	1999WO-IL00272	
BR 9910623A		WO 9959811	Based on
CN 1307522A	May 20, 1999	1999CN-0807808	
KR2001081960A	November 21, 2000	2000KR-0713075	

INT-CL (IPC): A01 N 25/26; A61 K 7/16; A61 K 7/18; A61 K 9/14; A61 K 9/50; A61 K 9/51; A61 K 33/00; A61 K 33/04; A61 K 33/10; A61 K 33/16; A61 K 33/38; A61 P 7/02; A61 P 9/00; A61 P 17/02; A61 P 17/10; B01 J 19/00; B32 B 5/16; C01 B 13/14; C01 B 33/12; C02 F 1/32; C09 K 3/00

ABSTRACTED-PUB-NO: WO 9959811A
BASIC-ABSTRACT:

NOVELTY - Ultradisperse nanoparticles of hydrated oxide for use in structuring biological media in a structure comprising (a) particle; (b) biological tissue and (c) surrounding media, the structured biological media comprising three-sided biological system.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for method of modifying surface of ultradisperse nanoparticles of hydrated oxides by partial methylation.

ACTIVITY - Bactericidal; cosmetic; dental.

USE - Used in structuring biological media (claimed). Used in toothpastes, to treat inflamed gum tissue, for direct delivery of fluoride to tooth enamel, in chewing gums for use as dentifrice, in medicinal, cosmetic, hygiene, agricultural, water-treatment and disinfection applications, and in the food industry (all claimed). Used in skin creams. Used in applications requiring radioactivity to reduce level of radioactivity needed thus reducing exposure. Used as safe and effective preservatives and stabilizers. Used to provide slow-release mechanisms. Used to increase sensitivity to antibiotic treatment, enabling more effective use of antibiotics at lower doses. Bind toxins released by infection to give general cleansing effect and reducing need to activate immune system giving body more strength to heal itself in shorter time. Used as hygienic body was h for all body cavities including surgical cavities. Used as exfolient cream to peel and absorb dead skin, to extract oil from skin pores without damage. Used in agriculture as biological exterminants. Used to deliver calcium fluoride to treat scars and keloids, magnesium to treat pruritis senilis, barium carbonate to treat cuprosis, sulfur and silicon dioxide to treat acne vulgaris and calcium sulfide to dissolve its scar tissue, silver nitrate as local disinfectant and to aid blood clotting with cauterizing effect on tissues for diabetic patients in whom healing process is especially slow, and zinc to treat balding caused by alopecia. Patients were treated with antibiotic alone or in presence of ultradisperse particles. Results for the following antibiotics alone or with particles, respectively, were as follows: penicillin 20 and 33; ampicillin 60 and 67; streptomycin 60 and 100; gentamycin 80 and 100; tetracycline 40 and 67; levomycitin 40 and 67; erythromycin 40 and 100 and kanamycin 80 and 100. The results show that, in all cases, sensitivity to antibiotics was boosted by use of ultradisperse particles.

ADVANTAGE - Surface structure of ultradisperse particles may be altered to allow predetermined interactions to take place in biological media. Sequential and/or

simultaneous actions may be performed by 'multi-action' particles. In skin creams, when skin is dry, oil is attracted to skin, and when skin needs water, water is attracted to skin, thus providing skin with treatment that it needs. Provide broad-spectrum bactericidal protection at lower concentrations than conventional preservatives and stabilizers. Particles reduce significantly amount of silica needed to function as preservative. Able to deal with different states in selective manner.

CHOSEN-DRAWING: Dwg.0/16

TITLE-TERMS: HYDRATED OXIDE STRUCTURE THREE SIDE BIOLOGICAL SYSTEM

DERWENT-CLASS: B07 C07 D13 D15 D21 D22 P73

CPI-CODES: B02-A; B02-E; B02-G; B02-P02; B02-T; B05-A01B; C02-E; C02-G; C02-P02; C02-T; C05-A01B; D08-A; D08-A05;

CHEMICAL-CODES:

Chemical Indexing M6 *01*
    Fragmentation Code
    M905 Q211 R034 R112

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C2000-013882
Non-CPI Secondary Accession Numbers: N2000-041460

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Freeform Search

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Term: L10 and (pharmaceut$ or cosme$ or agrichem$)

Display: 10 **Documents in Display Format:** - **Starting with Number** 1

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Search History

DATE: Monday, December 09, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB; PLUR=YES; OP=AND			
L12	L10 and (pharmaceut$ or cosme$ or agrichem$)	114	L12
L11	L10 and methylation	5	L11
L10	L9 and nanoparticle.clm.	321	L10
L9	l3 and (silica or titanium or aluminum)	1854	L9
DB=JPAB,EPAB,DWPI; PLUR=YES; OP=AND			
L8	l3 and (silica or titanium or aluminum)	80	L8
L7	l4 and (silica or titanium or aluminum)	1	L7
L6	l4 and prutrusion	0	L6
L5	L4	1	L5
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=AND			
L4	nanoparticle and methylation	189	L4
L3	nanoparticle	3889	L3
L2	L1	1859	L2
DB=USPT; PLUR=YES; OP=AND			
L1	nanoparticle	1859	L1

END OF SEARCH HISTORY

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=> d hist

     (FILE 'HOME' ENTERED AT 10:26:03 ON 09 DEC 2002)

     FILE 'REGISTRY' ENTERED AT 10:26:39 ON 09 DEC 2002
L1            25 S SILICON DIOXIDE
L2          2383 S ALUMINUM OXIDE
L3             1 S ALUMINUM TRIOXIDE
L4            42 S TITANIUM DIOXIDE
L5            68 S L4 OR L3 OR L1

     FILE 'CAPLUS, MEDLINE, BIOSIS' ENTERED AT 10:29:15 ON 09 DEC 2002
L6         22653 S NANOPARTICLE
L7             0 S NANO-PARTICULE
L8           842 S NANO-PARTICLE
L9           842 S NANO (W) PARTICLE
L10        23073 S L9 OR L8 OR L6
L11         3998 S L10 AND (SILICA OR TITANIUM OR ALUMINUM)
L12           53 S L11 AND (PHARMACEUT? OR COSMEC? OR AGRICULT? OR FOOD)
L13           51 DUPLICATE REMOVE L12 (2 DUPLICATES REMOVED)
L14          444 S SILICA (W) NANOPARTICLE
L15           20 S L14 AND HYDROPHOB?
L16           20 S L15 NOT L13
L17           19 DUPLICATE REMOVE L16 (1 DUPLICATE REMOVED)

=> s l14 and surface (w) modified
L18           21 L14 AND SURFACE (W) MODIFIED

=> s l18 not l16
L19           20 L18 NOT L16

=> s l19 and methylation
L20            0 L19 AND METHYLATION

=> s l19 and alkylation
L21            0 L19 AND ALKYLATION

=> s l19 and protrusion
```

L13 ANSWER 47 OF 51 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:491495 CAPLUS
DOCUMENT NUMBER: 121:91495
TITLE: Body distribution of 75Se-radiolabeled **silica nanoparticles** covalently coated with .omega.-functionalized surfactants after intravenous injection in rats
AUTHOR(S): Borchardt, G.; Brandriss, S.; Kreuter, J.; Margel, S.
CORPORATE SOURCE: Inst. Pharm. Technol., J.W. Goethe-Univ. Frankfurt, Frankfurt/M, D-60053, Germany
SOURCE: Journal of Drug Targeting (1994), 2(1), 61-77
CODEN: JDTAEH; ISSN: 1061-186X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Silica nanoparticles**, radiolabeled with 75Selenium, were coated with 14 types of .omega.-functionalized surfactants covalently bound to the particle surface. The particles were suspended in phosphate buffered saline (PBS) and injected i.v. via the tail vein of Wistar rats. The animals were sacrificed after 5 different time points (30 min, 2 h, 6 h, 24 h, and 7 d), and two samples of each organ and two blood samples were weighed into vials. The radioactivity of each sample was measured in a LKB-Wallac CliniGamma counter. Coated **silica nanoparticles** accumulated in the liver at much lower levels than other colloidal drug carriers after short time periods (30 min). The liver accumulation increased after longer time periods due to a natural redistribution process. Surface modification by increasing the hydrophilicity and thickness of coating yielded higher and longer persisting concns. in the intestine, blood, and the muscles. Initially increased lung concns. were decreasing with time, probably due to migration of the alveolar phagocytes.

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 1998:732910 CAPLUS
DOCUMENT NUMBER: 130:16558
TITLE: Nanoengineering of inorganic and hybrid hollow spheres by colloidal templating
AUTHOR(S): Caruso, Frank; Caruso, Rachel A.; Mohnwald, Helmuth
CORPORATE SOURCE: Max Planck Inst. Colloids Interfaces, Berlin, D-72489, Germany
SOURCE: Science (Washington, D. C.) (1998), 282(5391), 1111-1114
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hollow **silica** and **silica**-polymer spheres with diams. 720-1000 nm were fabricated by consecutively assembling **silica** **nanoparticles** and polymer onto colloids and subsequently removing the templated colloid either by calcination or decompn. upon exposure to solvents. SEM and TEM images demonstrate that the wall thickness of the hollow spheres can be readily controlled by varying the no. of **nanoparticle**-polymer deposition cycles, and the size and shape are detd. by the morphol. of the templating colloid. The hollow spheres produced are envisioned to have applications in areas ranging from medicine to **pharmaceutics** to materials science.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:131937 CAPLUS
DOCUMENT NUMBER: 128:258133
TITLE: Encapsulation of inorganic particles by dispersion polymerization in polar media. 1. **Silica nanoparticles** encapsulated by polystyrene
AUTHOR(S): Bourgeat-Lami, Elodie; Lang, Jacques
CORPORATE SOURCE: Inst. Charles Sadron (CRM-EAHP), Strasbourg, 67083, Fr.
SOURCE: Journal of Colloid and Interface Science (1998), 197(2), 293-308
CODEN: JCISA5; ISSN: 0021-9797
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polymer encapsulation of small silica particles, using dispersion polymn. of styrene in aq. ethanol medium with poly(N-vinylpyrrolidone) (PVP) as stabilizer, is described. Silica particles, directly synthesized by the Stober process in an aq. ethanol medium, are either unreacted (hydrophilic character) or coated with 3-(trimethoxysilyl)propyl methacrylate (MPS) (**hydrophobic** character), which is grafted at the silica particle surface. When the bare silica particles are used as the seed, there is a strong tendency of the silica beads to cover the surface of the polystyrene particles and obviously encapsulation does not occur. On the contrary, when the silica surface is made **hydrophobic** by coating, the inorg. particles are entirely contained in the polystyrene particles as evidenced by microscopy techniques (TEM, SEM, AFM). It is shown that some polystyrene chains are then chem. bonded to the silica particles, through the coupling agent MPS, and that only a small amt. of bonded polystyrene, compared to the total polystyrene synthesized, is sufficient to obtain encapsulation of the silica particles with the entire amt. of polystyrene synthesized during the polymn. Under our exptl. conditions, each polystyrene latex particle contains, on av., 4 to 23 silica beads depending, in particular, on the size of the silica. We believe that it is possible to control the composite particle size and morphol. by a convenient choice of the compn. of the system. Moreover, this new polymer-encapsulation process could be used to synthesize other org.-inorg. composite particles, using, for example, other monomers or minerals.

L13 ANSWER 48 OF 51 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 1994:316238 CAPLUS
DOCUMENT NUMBER: 120:316238
TITLE: Fluorimetric investigation of recombinant human growth hormone adsorbed on **silica nanoparticles**
AUTHOR(S): Clark, Steven R.; Billsten, Peter; Mandenius, C-F.; Elwing, Hans
CORPORATE SOURCE: Department of Physics and Measurement and Technology, Interface Biology Group, Linkoeping University, S-581 83, Linkoping, Swed.
SOURCE: Analytica Chimica Acta (1994), 290(1-2), 21-6
CODEN: ACACAM; ISSN: 0003-2670
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Since the introduction of recombinantly produced proteins (e.g., recombinant human growth hormone (rhGH)) for therapy, **pharmaceutical** companies have been searching for new techniques to investigate the solid surface-protein interaction and subsequently increase the shelf life of these mols. Deducing structural changes of proteins upon adsorption at a solid interface with fluorescence has been investigated to date mainly with total internal reflection fluorescence. Utilizing an unmodified spectrofluorimeter for investigation, the interaction of rhGH with hydrophilic **silica nanoparticles** (diam. 9 nm) is monitored through the intrinsic fluorescence of the rhGH's single tryptophan. General trends in the structural changes under different solvent conditions and different folded states are described.